

CLAIMS

1. An analogue or derivative of gastrin releasing protein (GRP) having Seq ID No. 2:
- 1 2 3 4 5 6 7 8 9 10 11
- 5 Xaa-Xaa-Leu-Xaa-Ala-Gly-Gly-Gly-Xaa-Val-Leu-
- 12 13 14 15 16 17 18 19 20 21 22
- Thr-Lys-Xaa-Tyr-Pro-Arg-Gly-Xaa-His-Trp-Ala-
- 10 23 24 25 26 27
- Val-Gly-His-Leu-Xaa
- wherein
- Xaa at position 1 is Val or pyroglutamic acid (Pyr),
- 15 Xaa at position 2 is Pro, Gly, Val, Ile, or Thr,
- Xaa at position 4 is Pro, Gly, Val, Ile, or Thr,
- Xaa at position 9 is Thr or Lys,
- Xaa at position 14 is Met or Leu,
- Xaa at position 19 is Asn or Lys,
- 20 Xaa at position 27 is Met or Leu,
- wherein the ϵ -amino group of one or more Lys is optionally substituted with a lipophilic substituent optionally via a spacer,
- or
- (a) a C-1-6-ester thereof,
- 25 (b) an amide, C-1-6-alkylamide, or C-1-6-dialkylamide thereof,
- (c) an Fmoc derivative thereof, and/or
- (d) a pharmaceutically acceptable salt thereof,
- except a peptide with the amino acid sequence having Seq. ID. No. 1
- 30 Val-Pro-Leu-Pro-Ala-Gly-Gly-Gly-Thr-Val-Leu-
- Thr-Lys-Met-Tyr-Pro-Arg-Gly-Asn-His-Trp-Ala-
- Val-Gly-His-Leu-Met
2. The analogue of gastrin releasing peptide (GRP) according to claim 1, wherein Xaa
- 35 at position 1 is pyroglutamic acid (Pyr).

3. The analogue of gastrin releasing peptide (GRP) according to claim 1, wherein Xaa at position 2 is Gly.
4. The analogue of gastrin releasing peptide (GRP) according to claim 1, wherein Xaa at position 2 is Val.
- 5 5. The analogue of gastrin releasing peptide (GRP) according to claim 1, wherein Xaa at position 4 is Gly.
6. The analogue of gastrin releasing peptide (GRP) according to claim 1, wherein Xaa at position 4 is Val.
7. The analogue of gastrin releasing peptide (GRP) according to claim 2, wherein the
10 total number of different amino acids between the gastrin releasing peptide (GRP) analogue and native gastrin releasing peptide (GRP) is five.
8. The analogue of gastrin releasing peptide (GRP) according to claim 2, wherein the total number of different amino acids between the gastrin releasing peptide (GRP) analogue and native gastrin releasing peptide (GRP) is four.
- 15 9. The analogue of gastrin releasing peptide (GRP) according to claim 2, wherein the total number of different amino acids between the gastrin releasing peptide (GRP) analogue and native GRP is three.
10. The analogue of gastrin releasing peptide (GRP) according to claim 2, wherein the
20 total number of different amino acids between the gastrin releasing peptide (GRP) analogue and native gastrin releasing peptide (GRP) is two.
11. The analogue of gastrin releasing peptide (GRP) according to claim 2, wherein the total number of different amino acids between the gastrin releasing peptide (GRP) analogue and native gastrin releasing peptide (GRP) is one.
12. The analogue of gastrin releasing peptide (GRP) according to claim 1, wherein Xaa
25 at position 9 is Thr.
13. The analogue of gastrin releasing peptide (GRP) according to claim 1, wherein Xaa at position 14 is Met.

14. The analogue of gastrin releasing peptide (GRP) according to claim 1, wherein Xaa at position 19 is Asn.
15. The analogue of gastrin releasing peptide (GRP) according to claim 1, wherein Xaa at position 27 is Met.
- 5 16. The analogue of gastrin releasing peptide (GRP) according to claim 1 having an amidated C-terminus, preferably -NH₂.
17. The derivative of gastrin releasing peptide (GRP) according to claim 1, wherein the ϵ -amino group of one or more Lys is substituted with a lipophilic substituent optionally including a spacer.
- 10 18. The derivative of gastrin releasing peptide (GRP) according to claim 17, wherein one or two Lys is substituted with a lipophilic substituent optionally via a spacer.
19. The derivative of gastrin releasing peptide (GRP) according to claim 18, wherein only one Lys is substituted with a lipophilic substituent optionally via a spacer.
20. The derivative of gastrin releasing peptide (GRP) according to claim 17, wherein the lipophilic substituent comprises from 4 to 40 carbon atoms, more preferred from 8 to 25 carbon atoms.
- 15 21. The derivative of gastrin releasing peptide (GRP) according to claim 17, wherein the lipophilic substituent comprises from 8 to 25 carbon atoms.
- 20 22. The derivative of gastrin releasing peptide (GRP) according to claim 17, wherein a lipophilic substituent is attached to an amino acid residue in such a way that a carboxyl group of the lipophilic substituent forms an amide bond with the ϵ -amino group of Lys.
- 25 23. The derivative of gastrin releasing peptide (GRP) according to claim 17, wherein the lipophilic substituent is attached to the parent peptide by means of a spacer.
- 30 24. The derivative of gastrin releasing peptide (GRP) according to claim 22, wherein the spacer is an unbranched alkane α,ω -dicarboxylic acid group having from 1 to 7 me-

thylene groups, preferably two methylene groups, which form a bridge between an amino group of the parent peptide and an amino group of the lipophilic substituent.

25. The derivative of gastrin releasing peptide (GRP) according to claim 22, wherein the spacer is an unbranched alkane α,ω -dicarboxylic acid group having two methylene groups, which form a bridge between an amino group of the parent peptide and an amino group of the lipophilic substituent.
26. The derivative of gastrin releasing peptide (GRP) according to claim 22, wherein the spacer is an amino acid residue except Cys, or a dipeptide such as Gly-Lys.
27. The derivative of gastrin releasing peptide (GRP) according to claim 24, wherein the ϵ -amino group of Lys forms an amide bond with a carboxylic group of the amino acid residue or dipeptide spacer, and an amino group of the amino acid residue or dipeptide spacer forms an amide bond with a carboxyl group of the lipophilic substituent.
28. The derivative of gastrin releasing peptide (GRP) according to claim 17, wherein the lipophilic substituent comprises a partially or completely hydrogenated cyclopentano-phenathrene skeleton.
29. The derivative of gastrin releasing peptide (GRP) according to claim 17, wherein the lipophilic substituent is a straight-chain or branched alkyl group.
30. The derivative of gastrin releasing peptide (GRP) according to claim 17, wherein the lipophilic substituent is the acyl group of a straight-chain or branched fatty acid.
31. The derivative of gastrin releasing peptide (GRP) according to claim 28, wherein the acyl group is selected from the group comprising $\text{CH}_3(\text{CH}_2)_n\text{CO}-$, wherein n is 4 to 38.
32. The derivative of gastrin releasing peptide (GRP) according to claim 28, wherein the acyl group is selected from the group comprising $\text{CH}_3(\text{CH}_2)_6\text{CO}-$, $\text{CH}_3(\text{CH}_2)_8\text{CO}-$, $\text{CH}_3(\text{CH}_2)_{10}\text{CO}-$, $\text{CH}_3(\text{CH}_2)_{12}\text{CO}-$, $\text{CH}_3(\text{CH}_2)_{14}\text{CO}-$, $\text{CH}_3(\text{CH}_2)_{16}\text{CO}-$, $\text{CH}_3(\text{CH}_2)_{18}\text{CO}-$, $\text{CH}_3(\text{CH}_2)_{20}\text{CO}-$ and $\text{CH}_3(\text{CH}_2)_{22}\text{CO}-$.

33. The derivative of gastrin releasing peptide (GRP) according to claim 17, wherein the lipophilic substituent is an acyl group of a straight-chain or branched alkane α,ω -dicarboxylic acid.
- 5 34. The derivative of gastrin releasing peptide (GRP) according to claim 30, wherein the acyl group is selected from the group comprising $\text{HOOC}(\text{CH}_2)_m\text{CO}-$, wherein m is from 4 to 38.
- 10 35. The derivative of gastrin releasing peptide (GRP) according to claim 30, wherein the acyl group is selected from the group comprising $\text{HOOC}(\text{CH}_2)_m\text{CO}-$, wherein m is from 4 to 24.
- 15 36. The derivative of gastrin releasing peptide (GRP) according to claim 30, wherein the acyl group is selected from the group comprising $\text{HOOC}(\text{CH}_2)_{14}\text{CO}-$, $\text{HOOC}(\text{CH}_2)_{16}\text{CO}-$, $\text{HOOC}(\text{CH}_2)_{18}\text{CO}-$, $\text{HOOC}(\text{CH}_2)_{20}\text{CO}-$ and $\text{HOOC}(\text{CH}_2)_{22}\text{CO}-$.
- 20 37. The derivative of gastrin releasing peptide (GRP) according to claim 17, wherein the lipophilic substituent is a group of the formula $\text{CH}_3(\text{CH}_2)_p((\text{CH}_2)_q\text{COOH})\text{CHNH}-\text{CO}(\text{CH}_2)_2\text{CO}-$, wherein p and q are integers and p+q is an integer of from 8 to 33.
38. The derivative of gastrin releasing peptide (GRP) according to claim 17, wherein the lipophilic substituent is a group of the formula $\text{CH}_3(\text{CH}_2)_p((\text{CH}_2)_q\text{COOH})\text{CHNH}-\text{CO}(\text{CH}_2)_2\text{CO}-$, wherein p and q are integers and p+q is an integer of from 12 to 28.
- 25 39. The derivative of gastrin releasing peptide (GRP) according to claim 17, wherein the lipophilic substituent is a group of the formula $\text{CH}_3(\text{CH}_2)_r\text{CO}-\text{NHCH}(\text{COOH})(\text{CH}_2)_2\text{CO}-$ wherein r is an integer of from 10 to 24.
- 30 40. The derivative of gastrin releasing peptide (GRP) according to claim 17, wherein the lipophilic substituent is a group of the formula $\text{CH}_3(\text{CH}_2)_s\text{CO}-\text{NHCH}((\text{CH}_2)_2\text{COOH})\text{CO}-$, wherein s is an integer of from 8 to 24.
- 35 41. The derivative of gastrin releasing peptide (GRP) according to claim 17, wherein the lipophilic substituent is a group of the formula $-\text{NHCH}(\text{COOH})(\text{CH}_2)_4\text{NH}-\text{CO}(\text{CH}_2)_u\text{CH}_3$, wherein u is an integer of from 8 to 18.

42. The derivative of gastrin releasing peptide (GRP) according to claim 17, wherein the lipophilic substituent is a group of the formula $\text{-NHCH(COOH)(CH}_2)_4\text{NH-COCH((CH}_2)_2\text{COOH)NH-CO(CH}_2)_w\text{CH}_3$, wherein w is an integer of from 10 to 16.
- 5 43. The derivative of gastrin releasing peptide (GRP) according to claim 17, wherein the lipophilic substituent is a group of the formula $\text{-NHCH(COOH)(CH}_2)_4\text{NH-CO(CH}_2)_2\text{CH(COOH)NH-CO(CH}_2)_x\text{CH}_3$, wherein x is an integer of from 10 to 16.
- 10 44. The derivative of gastrin releasing peptide (GRP) according to claim 17, wherein the lipophilic substituent is a group of the formula $\text{-NHCH(COOH)(CH}_2)_4\text{NH-CO(CH}_2)_2\text{CH(COOH)NH-CO(CH}_2)_y\text{CH}_3$, wherein y is zero or an integer of from 1 to 22.
- 15 45. A pharmaceutical composition comprising the analogue or derivative of gastrin releasing peptide (GRP) according to claim 1 and a pharmaceutically acceptable vehicle or carrier.
- 20 46. The pharmaceutical composition of claim 40, further comprising another antidiabetic agent.
47. The pharmaceutical composition of claim 41, wherein the antidiabetic agent is insulin.
- 25 48. The pharmaceutical composition of claim 41, wherein the antidiabetic agent is a hypoglycaemic agent.
49. The pharmaceutical composition of claim 41, wherein the antidiabetic agent is GLP-1 or an analogue or derivative thereof.
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